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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Yang et al.	37 C.F.R. § 1.8 Certificate of Mailing I hereby certify that this correspondence is today being deposited with the U.S. Postal Service in an envelope with appropriate postage affixed thereto and addressed to Commissioner for Patents and Trademarks, Washington, D.C. 20231. April 8, 2003 Theresa Doonan Recupido
Serial No.:	09/755,204	
Filing Date:	January 4, 2001	
Group Art Unit	1632	
Examiner	Deborah Crouch	
Title of Application:	METHOD FOR CLONING ANIMALS WITH TARGETED GENETIC ALTERATIONS	

April 8, 2003

Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

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SUPPLEMENTAL AMENDMENT

The following is in further response to the Office Action dated October 9, 2003 and supplements to the main amendment of March 25, 2003.

REMARKS

The applicants submit the following further comments in support of their earlier arguments that Cibelli et al. alone or in combination with other art does not teach or suggest the applicants' invention as presented in the amended claims which now recite that the population of cells is cultured through "at least five culturing passages."

Cibelli et al. utilized only briefly cultured cells for cloning. Attention is called to page 1256, column 3, lines 14-16 of the reference which recites "Fetal fibroblasts were isolated from a day 55 male fetus... cultured in vitro, and passaged twice before being..." and to column 3, lines 21-22 which recites, "cells were selected with neomycin for 2 weeks...." Thus in total, the Cibelli et al. cells were cultured less than 4 weeks.

Cibelli et al. have acknowledged that this brief culture is not sufficient for targeted genetic modifications as at page 1258, column 1, lines 4-9 they state that "the